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EXAMINER	
SNEDDEN, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,902	GAO ET AL.	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-64* is/are pending in the application.

4a) Of the above claim(s) *49-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-48 and 60-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. This Office Action is in response to Paper filed 8/25/2004. Claim 7 has been canceled. Applicant's amendment of claims 1, 8 and 63 is acknowledged. Claims 1-6, 8-48 and 60-64 are under examination.

Withdrawal of Objections and Rejections

2. The objections and/or rejections not explicitly restated or stated below are withdrawn.

Maintained Objections and Rejections

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-14, 18, 21-24, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al.* (US Patent 6,660,286) in view of Kunz *et al.* (US 2002/0025979).

Lambert teach a paclitaxel composition comprising a formulations for self-emulsifying systems of 0.1-20% paclitaxel, 10-90% Vitamin E (surfactant), 10-90% PEG 400 or N-methyl-2-pyrrolidone (solvent), 5-50% TPGS, 5-50% a secondary hydrophilific surfactant, such as Polysorbates (Tween 80), Pluronics (Pluronic F127), Cremophor RH40 (PEG-40 hydrogenated

castor oil) or Solutol HS-15 (see column 14, lines 21-32; regarding claims 1, 2, 4-6). Lambert *et al.* teach self-emulsifying systems of 0.1-20% paclitaxel and 10-90% of Vitamin E and other surfactants. A specific embodiment the composition of Lambert *et al.* would comprise 10% paclitaxel and 30-80% surfactant, allowing for a ratio of 1:3 to 1:8, for example. Ratios of 1:20 are also envisioned. (Regarding claims 7-8.) Lambert *et al.* teach the use of polyethylene glycol, PEG 400, as the solvent (regarding claims 9-11). For oral delivery, the paclitaxel composition is taught as being encapsulated in a water-soluble gelatin capsule (regarding claim 3 and 21). Thus, Lambert *et al.* expressly teach a composition of paclitaxel comprising a pharmaceutically acceptable surfactant (Vitamin E, TPGS, PEG-40 hydrogenated castor oil, Solutol HS-15) and a pharmaceutically acceptable solvent (PEG 400), contained in a gelatin capsule.

Lambert *et al.* does not teach the use of a substituted cellulosic polymer, such as HPMC, in the capsule wall, or as a binder or inactive filler within the capsule.

Kunz *et al.* teach an oral composition of Taxol, or paclitaxel. Kunz *et al.* teach the standard formulation present in the art as containing inactive ingredients such as cellulose, hydroxypropyl methylcellulose (HPMC) and microcrystalline cellulose (see Section [0168]; regarding claims 12-14, 18, 21-24). Hard or soft gelatin capsules containing paclitaxel can contain inactive ingredients, for example, gelatin and microcrystalline cellulose, as well as liquid vehicles such as polyethylene glycols (PEGs) and vegetable oil (see Section [0168]).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the HPMC in the composition of Kunz *et al.* for gelatin as a component of the capsule. Both gelatin and HPMC are water soluble compounds used in the art to encapulate pharmaceutical agents, such as paclitaxel as taught above. The person of ordinary

skill in the art with been motivated to use HPMC, and would have expected success, as HPMC is a routine and standard part of the oral capsule paclitaxel formulations. Hence, the substitution of HPMC for the gelatin of Lambert *et al.* represents the substitution of art-recognized or obvious equivalents in the preparations of paclitaxel capsules. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

5. Applicant's arguments filed 8/25/2004, have been fully considered but they are not persuasive. Applicant urges that neither reference alone or in combination teaches or suggests the claimed invention. Applicant urges that Kunz does not provide the necessary suggestion or motivation to use HPMC as the cellulosic polymer of the present invention. However, what the references do suggest is that a cellulosic polymer has the common and specific use of a major ingredient in the capsule wall of pharmaceutical compositions, that HPMC is commonly used for this specific purpose, and that use of HPMC in the capsule wall is a design choice or the routine optimization of a result-effective variable. Thus, it would have been obvious to use HPMC in the capsule wall of a paclitaxel tablet as taught by Kunz *et al.*

6. Claims 1, 2 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert *et al.* (US Patent 6,660,286) in view of Kunz *et al.* (US 2002/0025979) as applied to claims 1 and 2 above, and further in view of Broder *et al.* (US 6,395,770). Broder *et al.* oral doses of paclitaxel from 20 to 1000 mg/m^2 or about 2-30 mg/kg (see column 12, lines 25-50).

Broder *et al.* teach that this is the range for a therapeutically effective dose for paclitaxel responsive diseases.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to formulate paclitaxel at 10 to 700 mg/gm. A person of ordinary skill in the art would have been motivated to formulate an oral dose of paclitaxel at these concentrations in order to achieve a therapeutically effective to of paclitaxel. A person of ordinary skill in the art would have expected success when using paclitaxel at a dose of 10-700mg as it is known that a dose of 2-30 mg/kg is required to be effective in treating paclitaxel responsive disease. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

7. Applicant's arguments filed 8/25/2004, have been fully considered but they are not persuasive. Applicant urges that neither reference alone or in combination teaches or suggests the claimed invention. Applicant urges that Kunz does not provide the necessary suggestion or motivation to use HPMC as the cellulosic polymer of the present invention. Applicant argues Border *et al.* does not provide suggestion for the specific dosage of paclitaxel recited in the claims.

However, what the Kunz references does suggest is that a cellulosic polymer has the common and specific use of a major ingredient in the capsule wall of pharmaceutical compositions, that HPMC is commonly used for this specific purpose, and that use of HPMC in the capsule wall is a design choice or the routine optimization of a result-effective variable. Furthermore, as the invention is directed to pharmaceutical compositions of paclitaxel, dosage

would also be a design choice or the routine optimization of a result-effective variable, and as Border *et al.* teach a dosage within the range recited in the claims, the range is obvious.

New Rejections

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 18, 21-24, and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Straub *et al.* (US 6,610,317). Straub *et al.* teach a composition of paclitaxel, a surfactant, a solvent and a substituted cellulosic polymer. The surfactant of Straub *et al.* is taught as a surfactant or a wetting agent, and includes polyoxyethylene castor oil derivatives, for example (see column 3, line 7; column 4, lines 45 to column 5, line 40). The solvent of Straub *et al.* is taught as a solvent or a pore forming agent, and includes ethanol substantially removed to about 1%, for example (see column 2, column 6, lines 15 and 50). The substituted cellulosic polymer of Straub *et al.* is taught as cellulose dextran, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxy-propylmethyl cellulose, carboxyethyl cellulose, or carboxymethyl cellulose (column 4, lines 19-21).

Applicant's arguments filed 8/25/2004, have been fully considered but they are not persuasive. Applicant urges that Straub *et al.* does not expressly teach the specific ratio of paclitaxel:surfactant recited in amended claim 1. However, Straub *et al.* teach the elements of

the claim composition. The recitation of specific ratios add limitations that seek to optimize a result-effective variable to increase the solubilization of paclitaxel.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (571) 272-0959. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
November 10, 2004
SKS

JON WEBER
SUPERVISORY PATENT EXAMINER